Remarks

Claims 2-40 were previously pending in the subject application. By this amendment, the applicants have amended claims 3-5, 15-17, 28-34, 38, and 40. No new subject matter has been added by this amendment. Support for the amendments can be found throughout the application including, for example, at page 9, paragraph 32 of the subject specification. Accordingly, claims 2-40 are now before the Examiner for consideration. The amendments set forth herein should not be interpreted to indicate that the applicants have agreed with, or acquiesced to, the rejections set forth in the outstanding Office Action. Favorable consideration of the claims now presented, in view of the remarks and amendment set forth herein, is earnestly solicited.

Claim 38 was objected to for informalities. The applicants wish to thank the examiner for his helpful suggestions regarding the informalities identified. The applicants have revised claim 38 to clarify that the breath analyzer functions to analyze the patient's breath and provide a signal. Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

Claim 33 has been rejected under 35 U.S.C. §102(b) as being anticipated by Brown *et al.* (U.S. Patent No. 5,303,575). The applicants respectfully traverse the grounds for this rejection because the Brown *et al.* reference does not teach or suggest their claimed invention, which is directed to methods for measuring in exhaled breath endogenous compounds associated with medical conditions or diseases.

Brown *et al.* disclose a free-standing device that analyzes the amount of exogenous alcohol (namely ethyl alcohol) in a person's breath to determine blood-alcohol level. Throughout the patent, Brown *et al* describe analyzing exogenous alcohol levels for a user who has been consuming alcohol (see, for example, col. 1, lines 35-40; col. 7, lines 2-4; col. 11, lines 36-37 and 49-51; col. 16, lines 62-64; and col. 17, lines 17-20). There is no disclosure by Brown *et al.* regarding the analysis of endogenous compounds, let alone the concentration of endogenous alcohol in a person's breath.

In contrast, the subject invention measures endogenous alcohols in exhaled breath. Endogenous alcohols are produced by metabolism in the body and can normally be found in blood (see page 6, paragraph 17), as opposed to exogenous alcohols, which are derived from outside of the body (*i.e.*, via consumption). There is nothing in Brown *et al.* regarding monitoring endogenous

compounds associated with specific diseases or conditions. In fact, where a user has not consumed alcohol (*i.e.*, only endogenous alcohol is present in the body) and uses the Brown *et al.* device, the result that is displayed to the user is a zero value (see col. 16, line 51 through col. 17, line 2). Therefore, Brown *et al.* actually teach away from a device that measures endogenous alcohols in exhaled breath. Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra; Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

In *Dewey v. Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

> No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990; 52 USPQ 138 (2nd Cir. 1942).

As noted above, the Brown *et al.* reference does not disclose methods for analyzing endogenous compounds, such as alcohol, that are associated with medical conditions or diseases. Thus, the Brown *et al.* reference fails to describe each and every element of the subject invention. Under the applicable statutory and case law, the Brown *et al.* reference does not anticipate the

applicants' current claim. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §102(b).

Claims 33, 34, and 40 have been rejected under 35 U.S.C. §102(b) as being anticipated by Harte *et al.* (U.S. Patent No. 3,792,272). To the extent that this grounds for rejection might be applied to the newly amended claims, the applicants respectfully traverse this grounds of rejection because the Harte *et al.* reference does not teach or suggest the applicants' claimed method for monitoring endogenous compounds.

As with the Brown *et al.* patent, the Harte *et al.* patent describes systems and methods for analyzing the level of exogenous ethyl alcohol as well as detecting the presence of ketones in exhaled breath. The subject invention is directed to determining the concentration of endogenous alcohols in exhaled breath. Moreover, as noted above, claims 33, 34, and 40 have been amended to clarify the classes of endogenous compounds to be identified, namely to exclude ketones. Thus, none of the compounds recited in the claims are those detected by the Harte *et al.* device. Therefore, the Harte *et al.* reference fails to describe each and every element of the subject invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Claims 35-37 have been rejected under 35 U.S.C. §102(b) as being anticipated by Westenskow *et al.* (U.S. Patent No. 5,094,235). The applicants respectfully traverse the grounds for this rejection because the Westenskow *et al.* reference neither discloses nor suggests an apparatus that automatically controls the delivery of an anesthetic agent based upon the blood concentration of the administered anesthetic agent.

The Westenskow *et al.* device measures anesthetic agent concentrations in exhaled breath. There is no description or even suggestion by Westenskow *et al.* of using a breath analyzer in determining the concentration of the anesthetic agent in a patient's bloodstream. More importantly, Westenskow *et al.* fail to describe an anesthetic delivery system that controls the amount of anesthetic agent delivered to the patient based on the calculated blood concentration.

In contrast, the device of the subject application enables automatic, controlled delivery of an anesthetic agent based on analysis of a patient's breath to determine the concentration of the anesthetic agent in the patient's bloodstream. As noted in the subject specification at pages 16-18,

paragraphs 55-58, knowledge regarding the blood concentration of a delivered anesthetic agent is particularly important in maintaining satisfactory delivery of anesthesia during a medical or surgical procedure (*i.e.*, whether there is an accumulation of excess anesthetic agent in the blood). Since the Westenskow *et al.* device only measures the anesthetic concentration in exhaled breath without either determining the concentration of the anesthetic agent in the patient's bloodstream or controlling the supply of anesthesia based on the determined blood concentration level, it cannot reasonably anticipate the current invention. Accordingly, because the Westenskow *et al.* reference fails to describe each and every element of the subject invention, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Claim 39 has been rejected under 35 U.S.C. §102(b) as being anticipated by Georgieff (U.S. Patent No. 6,328,708). The applicants respectfully submit that Georgieff fails to describe a method for monitoring perflubron levels in an anemic patient by measuring the concentration of perflubron in exhaled breath.

Georgieff describes administering to a patient an inert gas, xenon, which is detectable in exhaled breath. An emulsion of xenon and perfluorocarbon compound are administered to a patient and the concentration of xenon is measured in exhaled breath (see col. 6, lines 58-64). In contrast, the subject invention describes measuring the concentration of perflubron, not an inert gas, in exhaled breath. Thus, the Georgieff reference fails to describe each and every element of the subject invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Claims 2, 3, 9, 18-20, 22, 23, 25, and 27-32 have been rejected under 35 U.S.C. §103(a) as being obvious over Jewett *et al.* (U.S. Patent No. 4,150,670) in view of Ueda *et al.* (U.S. Patent No. 5,573,005). The applicants respectfully traverse this ground for rejection because the cited references, alone or in combination, do not disclose or suggest the claimed methods.

In considering the patentability of the subject invention, it is very important to appreciate that the claimed invention is a method for determining the blood concentration of an agent based on the analysis of exhaled breath. As noted in the subject application, prior to the applicants' disclosure, blood concentration levels for an administered agent could only be determined via intrusive blood

testing. The subject invention advantageously analyzes exhaled breath for at least one substance indicative of an administered agent to determine the blood concentration of the agent and thus provide information regarding the depth of anesthesia (see page 7, paragraph 26, and Example 1 starting on page 16).

Jewett *et al.* disclose an automated closed system for delivering inhalation anesthetics. Jewett *et al.* only describe monitoring various known anesthetic factors such as expired anesthetic concentration. There is no description or suggestion by Jewett *et al.* of assessing patient blood level concentration of an administered agent.

The applicants respectfully submit that mere detection of expired anesthetic concentration would not provide information regarding the blood level concentration. As described in the subject application at page 16, paragraph 55, the "end tidal portion of exhaled breath is that fraction which has equilibrated with the blood returning from the systemic circulation to the lung." According to the subject invention, the concentration of an agent in exhaled breath must be analyzed to determine the blood level of the agent (*i.e.*, based on the end tidal portion of exhaled breath) to identify correctness of dosing, metabolism, and other pharmacokinetic deviations. In contrast, Jewett *et al.* fail to describe this very important step of determining blood level concentration. Thus, under these circumstances, the subject invention cannot reasonably be said to be obvious over Jewett *et al.*

The Ueda *et al.* reference merely discloses a method for collecting a sample of expired breath. Ueda *et al.* neither disclose nor suggest analyzing the sample of expired breath to determine the blood level concentration of an agent. Thus, the Ueda *et al* reference fails to remedy, or even address, the defects previously noted in Jewett *et al.* The skilled artisan would have had no reason to look to either the Ueda *et al.* reference or the Jewett *et al.* reference for guidance in developing a method for determining the blood level concentration of an administered agent based on the analysis of exhaled breath.

A finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. Here, it is only the applicants' disclosure that provides such a teaching, and the applicants' disclosure cannot be used to reconstruct the prior art for a rejection under 35 U.S.C.

§103. This was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969):

> The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 46 CCPA 905, 268 F.2d 226, 112 USPQ 364 (1959); *In re Sprock*, 49 CCPA 1039, 301 F.2d 686, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, in and of themselves and without the benefits of appellant's disclosure, make the invention as a whole, obvious. *In re Leonor*, 55 CCPA 1198, 395 F.2d 801, 158 USPQ 20 (1968). (Emphasis in original)

The mere fact that the purported prior art could have been modified or applied in a manner to yield applicant's invention would not have made the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Moreover, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art . . . ." *In re Dow Chemical Co., supra* at 1531. In either the Jewett *et al.* reference or the Ueda *et al.* reference, one finds neither. The applicants respectfully submit that any suggestion to determine agent blood level concentration based on analysis of exhaled breath could only be arrived at through hindsight reconstruction, which is improper. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Claims 4-8, 10-17, 21, and 24 have been rejected as obvious over Jewett *et al.* in view of Ueda *et al.* and Struys *et al.* (U.S. Patent No. 6,599,281). The applicants again respectfully traverse this ground for rejection because the cited references, alone or in combination, do not disclose or suggest the advantageous method for determining blood level concentration of the current invention.

The shortcomings of the Jewett *et al.* and Ueda *et al.* references have been discussed above in detail. Struys *et al.* disclose monitoring a wide range of physiologic variables (*i.e.*, EEG or EKG) for use in controlling the delivery of medication to a patient. Struys *et al.* fail to describe or even suggest determining the blood level concentration of an agent by analyzing exhaled breath. For example, Struys *et al.* describe using bispectral analysis of the patient's EEG to monitor the effect of an anesthetic on a patient (see col. 8, lines 51-54). In fact, to assess pharmacological (and

pharmacodynamic and pharmacokinetic) effects of a drug, Struys *et al.* describe assessing EEG and arterial pressure (see col. 14, lines 19-25) as well as population modeling (see col. 19, lines 48-54). Struys *et al.*'s emphasis on using a variety of indirect measurements, such as EEG and population modeling, effectively teaches away from the methods of the current invention, which provides direct measurement of blood level concentration. Thus, when the Struys *et al.* reference is read in conjunction with the teachings of Jewett *et al* and Ueda *et al.*, the prior art, when read as a whole, teaches away from determining the blood level concentration of an agent via analysis of exhaled breath (*i.e.*, based on the end tidal portion of exhaled breath).

As noted above, a finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. The cited references, alone or in combination, provide no motivation to modify the cited teachings without the guidance of the applicants' disclosure. Without such a motivation, no *prima facie* case of obviousness has been made. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection set forth under 35 U.S.C. §103.

Claim 20 has been rejected as obvious over Jewett *et al.* in view of Ueda *et al.* and Lewis *et al* (U.S. Patent No. 6,244,096). The applicants respectfully traverse this grounds for rejection because the cited references do not disclose or suggest the claimed invention.

The shortcomings of the Jewett *et al.* and Ueda *et al.* references have been discussed above in detail. The Lewis *et al.* reference discloses systems and methods for detecting the presence of and quantitating an anesthetic agent in exhaled breath (see col. 13, lines 1-12). There is no description or suggestion by Lewis *et al.* of assessing patient blood level concentration of an administered agent. As noted above, the mere detection of expired concentration of an agent would not provide information regarding the actual blood level concentration of the agent. Thus, the Lewis *et al.* reference fails to remedy, or even address, the defects previously noted in either the Jewett *et al.* or Ueda *et al* references. Under these circumstances, the subject invention cannot reasonably be said to be obvious over Jewett *et al* in view of Ueda *et al.* and Lewis *et al.* Moreover, one of ordinary skill in the art would have had no motivation to modify the cited references without the guidance of the

applicants' disclosure. Accordingly, because a *prima facie* case of obviousness has not been raised, reconsideration and withdrawal of the rejection of claim 20 is respectfully requested.

Claim 26 has been rejected as obvious over Jewett *et al.* in view of Ueda *et al.* and Psaros *et al.* (U.S. Patent No. 5,501,212). The applicants respectfully traverse this grounds for rejection because the cited references neither disclose nor suggest the claimed invention.

The shortcomings of the Jewett *et al.* and Ueda *et al.* references have been discussed above in detail. Psaros *et al.* describe a heat-moisture exchanger, which is used during anesthesia to prevent excessive drying of the patient's respiratory tract during delivery of an inhalation agent. There is no disclosure or suggestion by Psaros *et al.* to determine patient blood level concentration of an administered agent via analysis of exhaled breath. Accordingly, because the cited references, alone or in combination, do not disclose or suggest the advantageous method for determining patient blood level concentration of the current invention, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §103.

As a final matter, claim 38 has been rejected under 35 U.S.C. §103(a) as being obvious over Struys *et al.* in view of Westenskow *et al.* The applicants respectfully traverse this grounds for rejection because the cited references neither disclose nor suggest the claimed apparatus.

The shortcomings of the Struys *et al.* and Westenskow *et al.* references have been discussed in detail above. As noted earlier, Westenskow *et al.* fail to teach a breath analyzer that provides a signal indicative of the concentration of the anesthetic agent in blood, nor do they describe a delivery system with a controller that automatically delivers the appropriate amount of anesthetic agent to the patient based on the calculated blood concentration.

Struys *et al.* fail to remedy, or even address, the defects noted in the Westenskow *et al.* reference. There is no description or even suggestion by Struys *et al.* of using a breath analyzer in determining the concentration of the anesthetic agent in blood. Only indirect parameters (*i.e.*, EEG; EKG; population modeling) are used by Struys *et al.* in controlling the delivery of medication to a patient. As noted earlier, Struys *et al.*'s emphasis on using indirect measurements, such as EEG and population modeling, effectively teaches away from the methods of the current invention, which utilize analysis of exhaled breath to determine blood level concentrations. Thus, when the Struys *et*

al. reference is read in conjunction with the teachings of Westenskow *et al.*, the prior art, when read as a whole, teaches away from the apparatus of the current invention. Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) is respectfully requested.

In view of the foregoing remarks and amendment, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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